EAHP Survey 2010 on hospital pharmacy in Europe: Part 3. Production and quality assurance

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The number of hospital pharmacies in Europe producing sterile as well as non-sterile medicines has decreased significantly since 2000. In addition, the number of pharmacies preparing total parenteral nutrition, cytotoxics and intravenous admixtures (24.6%, 43.8% and 8.0% of pharmacies, respectively) is quite low and depends to a large extent on the size of the pharmacies, with larger units generally demonstrating significantly higher production activity. There are some differences between eastern and western Europe. Quality control and good manufacturing practice (GMP) seem to be well implemented (61.3% of pharmacies have adopted GMP) and many pharmacies have external certification.

Introduction

The pan-European survey of hospital pharmacy practice conducted by the European Association of Hospital Pharmacists (EAHP) is an important source of information for understanding future professional challenges and system development needs in Europe. The methodology and the background of the 2010 survey were previously described in this journal.[1] In this article we present the production and quality assurance findings.

Results

In general, the number of hospital pharmacies across Europe producing medicines for stock and for individual prescriptions has decreased substantially since 2000 (figure 1).[2] This is especially the case for the production of stock sterile medicines, which the 2010 survey shows to be less than half of that recorded in the 2000 survey (decreasing from 66.8% to 29.9% of pharmacies). However, the 2010 survey also recorded a 32% decrease (from 71.0% to 48.5% of pharmacies) since 2000 in pharmacy involvement in the production of individual sterile preparations. Production for all preparations is highly dependent on the size of the hospital (table 1) with the larger units recording significantly more production activity.

While reagents for laboratories are seldom produced in hospital pharmacies (16.5% of pharmacies), production of non-sterile medicines is common, especially for individual prescriptions (65.8 of pharmacies). Across Europe, only 43.8% of pharmacies reconstitute cytotoxics: this practice occurs in around 80% of large hospitals but in <20% of small hospitals (as they may not need this service). Centralisation of admixtures is still quite low (max. 8.5% of pharmacies for all units and 23.5% for special units) but in contrast compounding of total parenteral nutrition (TPN) seems to be well developed (64.7% of the very large hospitals). This is not surprising considering the high costs of the facilities needed in particular for the aseptic production.

As regards determining the cost-effectiveness of production, 77.5% of pharmacies record the costs of the raw materials (n=920) and 42.7% labour costs, while only 23.7% take into consideration equipment depreciation and 28.4% quality control costs. Regulations across Europe in relation to hospital pharmacy production differ and a licence to supply own products to other hospitals is not mandatory in all countries. Only 18.5% of pharmacies supply other hospitals (n=999) and 41% of these do so in order to generate hospital revenue (n=159).

There are also some differences between eastern and western Europe, particularly as regards licences for in-house production and manufacture for other hospitals and outpatients (table 2).

In eastern Europe, only in the Czech Republic and Hungary are a large number of pharmacies (57.1% and 57.4%, respectively) licensed to produce investigational medicinal products (IMPs). In western Europe, Denmark (100%), Sweden (81.3%) and Spain (62.7%) have the highest percentages of IMP licences. Very few hospital pharmacies are involved in advanced therapies and only 1.9% have a gene therapy licence. Only Austria, Denmark, Germany, Hungary, Italy, Norway, Portugal and Spain have issued such licences, with Denmark having the most (28.6%)

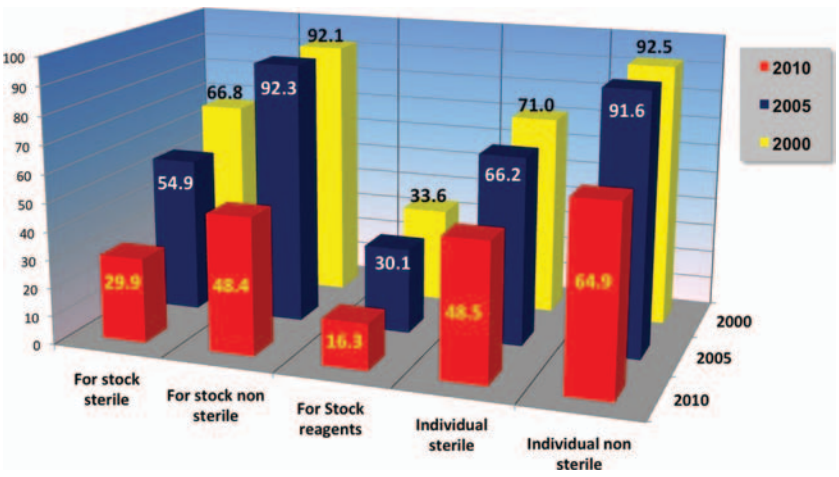

Figure 1 Production of medicines in hospital pharmacies: percentages of pharmacies producing medicines for stock (n=982) and for individual prescriptions (n=988).

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Table 1 Percentage of pharmacies producing medicines for stock (n=982) and for individual prescriptions (n=988)

	Production for stock			Production for individual prescriptions					
Hospital size (by number of beds)	Sterile products	Non-sterile products	Reagents	Sterile products	Non-sterile Products	TPN	Cytotoxics	Intravenous admixtures for all units	Intravenous admixtures only for special units (eg, ICU)
All hospitals	30.4	49.3	16.5	48.6	65.8	24.6	43.8	2.7	8.0
1–49	0.0	7.7	0.0	7.7	7.7	0.0	15.4	0.0	0.0
50–99	0.0	11.6	2.3	9.1	22.7	2.3	11.4	0.0	0.0
100–199	5.7	22.9	4.3	15.6	37.6	9.2	12.8	1.4	2.1
200–299	12.9	37.6	8.9	27.1	50.5	9.0	23.4	0.9	2.7
300–399	21.2	44.9	12.7	41.4	62.9	16.8	33.6	2.5	1.7
400–599	31.1	50.9	13.0	50.3	74.5	20.6	48.1	2.5	5.6
600–799	27.8	49.5	12.4	57.1	72.4	25.3	51.5	1.0	9.1
800–999	45.6	61.4	15.8	64.9	80.7	40.7	62.7	6.8	11.9
1000–1499	58.8	73.9	28.6	81.5	89.9	45.7	72.4	5.2	18.1
1500–2000	66.0	85.1	48.9	91.5	95.7	51.1	78.7	8.5	23.4
>2000	73.1	86.5	50.0	88.5	92.3	64.7	84.3	2.0	23.5

n=997 respondents for cytotoxics and intravenous admixtures.
TPN, total parenteral nutrition.

licensed pharmacies. Only oncology hospitals are involved in advanced therapy (6.3%).

Quality of production is high as 61.3% of pharmacies reported that GMP has been implemented (n=949) and 64.4% have a written procedure for the recall of their own products (n=964). However, the situation differs by country (figure 2). For example, there is quite a gap between some countries (Denmark, Finland, Sweden and UK) and eastern Baltic countries, where only a few hospitals have implemented GMP, possibly because of economic constraints.

Awareness of quality control and assurance is also demonstrated by the high number of hospital pharmacies who have achieved certification (figure 3). Due to the existence of other implemented certification systems, in some countries such as France and Belgium ISO certification is

Table 2 Percentage of pharmacies with a production licence (n=972)

	Inpatients		Outpatients and other hospitals			
Country	Sterile products	Non-sterile products	Sterile products	Non-sterile products	Medicines for clinical trials	Gene therapy
All countries	44.0	65.7	19.0	24.0	30.5	1.8
Austria	76.5	88.2	32.4	29.4	52.9	8.8
Belgium	57.1	71.4	14.3	14.3	48.6	0.0
BiH	16.7	83.3	0.0	0.0	16.7	0.0
Bulgaria	7.3	45.5	0.0	3.6	0.0	0.0
Croatia	27.5	75.0	0.0	0.0	5.0	0.0
Czech Republic	69.0	97.6	45.2	76.2	57.1	0.0
Denmark	100	100	85.7	85.7	100	28.6
Estonia	11.1	83.3	5.6	11.1	11.1	0.0
Finland	42.9	52.4	14.3	14.3	19.0	0.0
France	46.2	50.0	15.4	15.4	26.9	0.0
FYROM	18.8	43.8	6.3	0.0	6.3	0.0
Germany	43.9	50.0	13.3	16.3	26.5	2.0
Greece	43.3	80.0	30.0	56.7	50.0	0.0
Hungary	42.6	83.0	14.9	40.4	57.4	4.3
Ireland	0.0	3.3	0.0	0.0	0.0	0.0
Italy	44.7	50.0	19.3	21.1	24.6	4.4
Latvia	21.4	60.7	0.0	0.0	0.0	0.0
Lithuania	50.0	75.0	0.0	0.0	25.0	0.0
Luxembourg	60.0	80.0	20.0	40.0	20.0	0.0
Netherlands	54.5	72.7	45.5	54.5	45.5	0.0
Norway	100	93.8	68.8	75.0	56.3	6.3
Poland	39.3	85.7	7.1	14.3	14.3	0.0
Portugal	60.0	64.0	28.0	36.0	44.0	4.0
Serbia	14.3	46.4	0.0	0.0	17.9	0.0
Slovakia	24.1	94.8	0.0	3.4	17.2	0.0
Slovenia	30.4	60.9	8.7	21.7	30.4	0.0
Spain	86.4	93.2	50.8	57.6	62.7	3.4
Sweden	93.8	68.8	81.3	68.8	81.3	0.0
Switzerland	72.2	72.2	27.8	27.8	38.9	0.0
UK	35.7	7.1	35.7	7.1	28.6	0.0

BiH, Bosnia-Herzegovina; FYROM, former Yugoslav Republic of Macedonia.

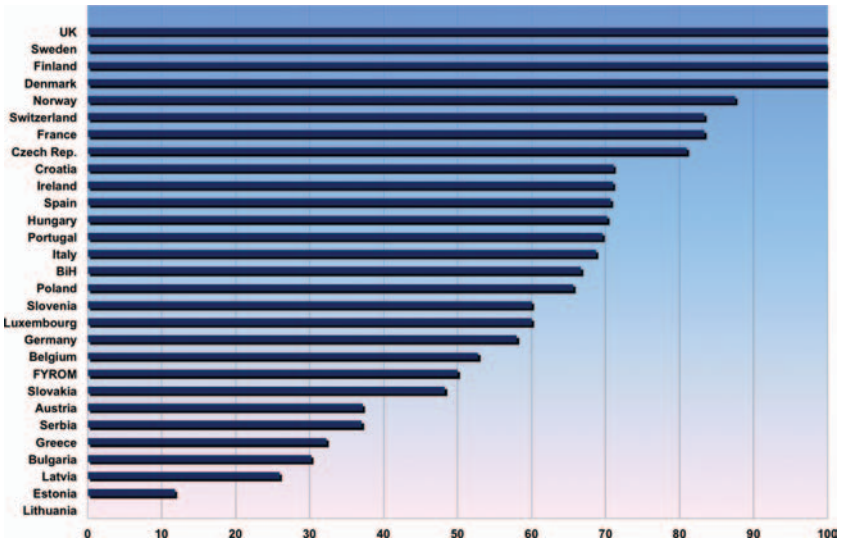

Figure 2 Percentage of pharmacies implementing good manufacturing practice (GMP) by country (n=949). BiH, Bosnia-Herzegovina; FYROM, former Yugoslav Republic of Macedonia.

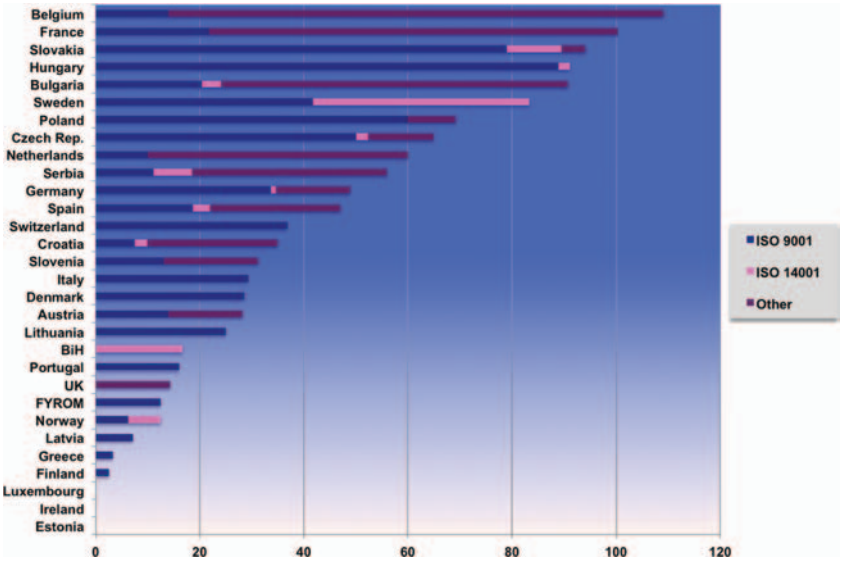

Figure 3 External certification (%) by country (n=973). Total may be >100% as some pharmacies have two different certificates. BiH, Bosnia-Herzegovina; FYROM, former Yugoslav Republic of Macedonia.

not the most commonly used accreditation standard, and, at least in Belgium, some pharmacies have two certificates (which explains the total percentage being >100%). There are large differences across Europe with some countries (Estonia, Ireland and Luxembourg) having no certification according to our data.

The survey suggests that the presence of quality control systems is highly dependent on the size of the hospital in question (table 3, n=986), with large hospitals more commonly having such systems. The quality control of chemical and physical elements is generally less robust than that of microbiological stability. Raw materials and finished products are well tested (67.3% and 67.9% of pharmacies, respectively) with packaging material less so (22.3%). In general the tests are performed in the pharmacy (67.3% of pharmacies) but also at external locations (67.9%) or in other laboratories of the same hospital (22.3%).

Limitations

In addition to some of the previously discussed and accepted limitations of the EAHP survey,[1] since 2005 a number of eastern countries with low hospital pharmacy production and quality control have joined EAHP. This may have created a bias by increasing the true decline in such activities. Also the results concerning GMP are surprising and should be treated with caution; it is possible that some respondents may have misinterpreted the term 'GMP' (which means fulfilling the EU directive) as meaning a more general 'best practice'.

Discussion

The decrease in the numbers of hospital pharmacies involved in sterile batch production could be due to increased

Table 3 Percentage of pharmacies (n=986) implementing quality control measures

	Quality control			Test performed					
Hospital size (by number of beds)	Chemical stability	Physical stability	Micro-biological stability	On raw materials	On packaging material	On finished product	In the pharmacy	In other hospital laboratory	External laboratory
All hospitals	25.3	25.9	41.8	67.3	22.3	67.9	67.3	22.3	67.9
1–49	0.0	0.0	0.0	NA	NA	NA	NA	NA	NA
50–99	6.8	6.8	11.4	100	0.0	0.0	100	0.0	0.0
100–199	6.5	8.0	18.1	56.3	18.8	46.9	56.3	18.8	46.9
200–299	15.7	19.4	25.9	62.9	14.3	51.4	62.9	14.3	51.4
300–399	17.1	20.5	32.5	72.7	20.5	52.3	72.7	20.5	52.3
400–599	17.5	17.5	45.6	61.7	11.1	66.7	61.7	11.1	66.7
600–799	23.7	26.8	48.5	64.0	24.0	70.0	64.0	24.0	70.0
800–999	32.2	33.9	57.6	56.3	21.9	65.6	56.3	21.9	65.6
1000–1499	50.4	48.7	63.9	65.9	26.4	80.2	65.9	26.4	80.2
1500–2000	59.6	55.3	72.3	83.8	35.1	73.0	83.8	35.1	73.0
>2000	66.7	58.8	74.5	81.6	32.7	83.7	81.6	32.7	83.7

n=463 respondents for type of material tested and n=471 respondents for laboratory location. Multiple answers are possible.
NA, not applicable (no data).

reliance on industrial manufacture, as well as the concentration of production in larger hospital pharmacies. There are similar decreases in production activity in relation to individual preparations, at least for small and medium-sized hospitals. This development is regrettable in light of the needs of personalised medicine and the fact that only pharmacists are competent within hospitals to create such preparations. Nevertheless, the EAHP survey did not seek information about the outsourcing of production, which might have been relevant in terms of the results. It is also surprising that only 43.8% of the pharmacies surveyed offered centralised cytotoxic reconstitution. Even though only some hospitals are involved in oncology, this percentage is low with only 53.1% of oncology hospitals offering such a service (data not shown). We were unable to determine from the survey results whether this is the result of outsourcing or of reconstitution in the ward, both of which practices contravene the recommendations of the International Pharmaceutical Federation (FIP) Basel statements of 2008.[3] Also the preparation of intravenous admixtures needs to be improved as they can be very sensitive microbiologically and should therefore be prepared in the pharmacy as suggested in Basel statement 36.[3] The low percentage of hospital pharmacies meeting this standard (max 23.5%) is therefore unsatisfactory.

Our data show that hospital pharmacies are not yet ready to prepare advanced medicines. This is not yet an acute need but may be so in the future. As regards personalised medicines, preparation competencies within hospital pharmacies should be maintained.

Hospital pharmacies in Europe in general show a good understanding of quality control and assurance and have often achieved external certification. Nevertheless, the need to meet GMP requirements in the future may challenge some small pharmacies and the trends towards concentration in larger production facilities—as suggested by our results from 2000 and 2005—will probably continue.

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